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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: DHAR et al.	Group Art Unit: 1641
Serial No.: 09/779,455	Examiner: Bao-Thuy L. Nguyen
Filed: 9 <sup>th</sup> February 2001	
For: <i>A highly cost-effective analytical device for performing immunoassays with ultra high sensitivity</i>	Attorney Docket No: 056859/0115

To,  
The Assistant Commissioner for Patents  
Washington, D.C. 20231

Declaration Under 37 C.F.R. § 1.132

I, Tarun K. Dhar age 50 years, residing at INDIA, and a citizen of India, do hereby state as under.

I am a Scientist at the Indian Institute of Chemical Biology, Jadavpur, Calcutta, India. I graduated in the year 1973 from Lucknow University located at Lucknow, INDIA. I completed my Master's Degree in Organic Chemistry from Lucknow University at Lucknow, INDIA in the year 1975. Subsequently, I completed my doctoral degree in Chemistry from Calcutta University, Calcutta, India in the year 1980.

I took up my first assignment as a SSA with the Indian Institute of Chemical Biology, Calcutta in the year 1979. After that, I joined the same Institute as in year 1981 as

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Scientist where I am continuing to now work on Immunochemistry for the last 24 years. Presently, I am working as Scientist F at this institute.

I am fully aware of the prosecution history of this case and am in receipt of the final office action issued by U.S. PTO.

I hereby state the invention of the instant application is totally non-obvious against the cited arts. The Examiner himself agrees that Brown *et al* does not teach any absorbent material. Further, the Examiner must appreciate that Lin *et al* talks about using blotting papers for blotting dry the spot. Thus, the blotting paper is used in dry form and the purpose is to dry the spot. Whereas, the absorbent of the instant Application is a pre-wetted absorbent. Also, the purpose of the pre-wetted absorbent is entirely distinct from that of the Lin *et al*.

The wetted absorbent body facilitates in the adherence of the membrane strips to the absorbent body and maintains the continuity of capillary channels with fluid receiving zone. It is important that there is no air bubble between the membrane and absorbent body and both are in intimate contact with each other, as air bubbles interfere with the fluid flow through the membrane. The void volume of the wetted absorbent body is sufficient to absorb the additional fluid introduced during the assay. As a result, the applied fluid is efficiently absorbed by the absorbent body through antibody-immobilized zones within few seconds without application of any force. As there is very little lateral diffusion, costly-labeled reagents can be used efficiently.

Optimal wetting of the absorbent body is essential as it has considerable influence on the sensitivity of the assay. The water content can be controlled by using either of the methods described in the experimental and needs to be between 1.4 to 1.8 ml for a 90 X 56 mm filter paper (approximately 1.4 - 1.8 ml / gm) for good results. The water content

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of such a filter paper prepared by rolling a test tube by four different operators were consistently found to be within this range. If excess water is removed, the contact between the membrane and the absorbent body becomes insufficient and non-uniform. Excess wetting (2 ml/gm) of the absorbent body reduces the flow rate thereby allowing the fluid to spread laterally resulting in gradual decrease in spot intensities in the order a to d.

Now, there is no clue for the Applicant from any of the cited arts to use pre-wetted absorbent. This is especially in view of the fact that the benefits of using pre-wetted absorbent are absent in all the cited arts. So, there is no motivation for the Applicants to use pre-wetted absorbent.

On the contrary, the object of using the blotting paper in Lin *et al* is to dry the spot. Thus, the very objects of the use of absorbent material in two works are totally distinct. Thus, it would not be appropriate to consider the instant device unpatentable over Brown *et al* in view of Lin *et al*. Similarly, it would be so for Kearns *et al* in view of Lin *et al* and Bhattacharya *et al*.

In addition, the analytical device developed in the present invention is non-obvious over Lin *et al* in following respect: a) The reaction membrane is hydrophilic and membrane surface is used for immobilization of antigen or antibody. b) Applied sample and reagents over spotted antigen or antibody zone of the reaction membrane passes to the absorbent body through immunofiltration and thereby reduces the assay time whereas in Lin's device dry absorbent body is used for blotting dry after washing. c) Absorbent body is not used after washing, rather we use absorbent body made of cellulose acetate, filter paper or bathroom tissue paper before washing to absorb the sample or reagents for immunofiltration-based assay under wet state.

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Further, the absorbent body of the instant application under wet state facilitates close intimate contact with the reaction membrane and form the capillary channels to allow fast transfer of applied fluid over spotted zones of the reaction membrane to the absorbent body. However, this is not the case with the cited arts.

We recognize that the Examiner objection is an objection of obviousness, and we have addressed this objection of obviousness adequately earlier. Yet, we would respectfully submit that there is no inspiration or clue from the each document to seek support for other documents or other areas of knowledge. Each document is stand-alone and there is no logical link between one document to another document. In short, both fall in different directions and the present invention provides yet another direction, which has no bearing on the citations. They are individual patents and there is no motivation to continue. Whereas, the instant invention is made with a progressive approach and not with hindsight.

Had it been obvious, the invention would have taken place immediately after the cited arts. There are several research groups in various parts of the world that are active in this area of research. Had it been so obvious, they would not have waited for the instant invention. This can be further substantiated by the fact that, the Applicant has an understanding with a Multinational Company to commercialize the device of the instant Application. Had it been obvious, then the diagnostic and pharmaceutical industries would have come out with the instant device long back.

Further, unless one actually conducts the experiments, the person cannot be sure about achieving the desired result. The inventors have conducted multiple experiments of varying nature. It is only after several years of hard work involving much human involvement and inventive skills that the inventors have been able to achieve the desired results.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that

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these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Dated: 16.02.2004

Place: Kolkata

*Tarun Kumar Dhar*  
TARUN K. DHAR